Established and potential predictors of blood loss during lung transplant surgery

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Abstract: Lung transplantation is an established therapeutic procedure for end stage lung diseases. Its success may be impaired by perioperative complications. Intraoperative blood loss and the resulting blood transfusion are among the most common complications. The various factors contributing to increased blood loss during lung transplantation are only scarcely investigated and not yet completely understood. This is in sharp contrast to other surgical fields, as in orthopedic surgery, liver transplantation and cardiac surgery the contributors to blood loss are well identified. This narrative review article aims to highlight the acknowledged factors influencing blood loss in lung transplantation (such as double vs. single lung transplant) and to discuss potential factors that may be of interest for further research or helpful to develop strategies targeting risk factors in order to minimize blood loss during lung transplantation and finally improve patient outcome.

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Review Article

Established and potential predictors of blood loss during lung transplant surgery

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Abstract: Lung transplantation is an established therapeutic procedure for end stage lung diseases. Its success may be impaired by perioperative complications. Intraoperative blood loss and the resulting blood transfusion are among the most common complications. The various factors contributing to increased blood loss during lung transplantation are only scarcely investigated and not yet completely understood. This is in sharp contrast to other surgical fields, as in orthopedic surgery, liver transplantation and cardiac surgery the contributors to blood loss are well identified. This narrative review article aims to highlight the acknowledged factors influencing blood loss in lung transplantation (such as double vs. single lung transplant) and to discuss potential factors that may be of interest for further research or helpful to develop strategies targeting risk factors in order to minimize blood loss during lung transplantation and finally improve patient outcome.

Keywords: Blood loss; lung transplant surgery; patient blood management

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Introduction

The first successful lung transplantation has been performed in 1983 (1). Since then it is the ultimate therapeutic option for inherited or acquired end stage lung diseases such as cystic fibrosis (CF), primary pulmonary arterial hypertension and pulmonary fibrosis, if maximum medical and surgical strategies fail (2).

Common complications after lung transplantation are early graft dysfunction (primary graft dysfunction (PGD), renal failure (3), infections (4) and blood loss (5), the latter being influenced by various factors in thoracic surgery (6). Infections and renal failure are not only adverse effects after lung transplant, but also acknowledged risk factors for decreased 1-year survival after lung transplantation (7). Growing evidence underlines that blood transfusions are causing adverse effects (8). Patient blood management aims to minimize allogeneic blood transfusions in order to save cost and prevent negative consequences (9,10). Examples for the latter are transfusion-associated circulatory overload (TACO) (11), PGD (12) and transfusion-related acute lung injury (TRALI) (13). Nowadays, blood transfusions are acknowledged to prolong hospital stay and increase mortality after lung transplantation (14). In addition, the direct economic effect should not be underestimated as the cost of one unit of packed red blood cells (PRBC) in the United States ranges between US$700–1,200 (15). Therefore, predicting, evaluating, and finally reducing blood loss in lung transplantation might contribute to lower cost, reduced morbidity and better survival.

Predictors of blood loss in other surgical procedures

Identifying predictors of blood loss is usually not the goal *per se*. However, predictors of blood loss may contribute to make surgery more efficient and finally to reduce the amount of required transfusions.

Orthopedic surgery

In orthopedic surgery, Park *et al.* identified male sex, preoperative autologous blood donations, and a Charlson comorbidity score of >3 to be independently linked to an increased perioperative blood loss in both total knee arthroplasty and total hip arthroplasty (16). In total hip arthroplasty, regional anesthesia was associated with reduced blood loss (16). While it is clear, that some of the predictors mentioned might not be influenced (e.g., the patient's gender), others can be adapted easily, for example the type of anesthesia applied.

Liver surgery

For liver surgery, independent predictors of blood loss and blood transfusion include preoperative hematocrit, low platelets, and a high INR (17). Other studies have described a body mass index (BMI) of ≥23 kg/m^2, low prothrombin activity amongst others to be predictive for blood loss (18-20). In particular in orthotopic liver transplantation, Mangus *et al.* identified age, MELD (model of end-stage liver disease) score, preoperative hemoglobin, initial fibrinogen, initial central venous pressure, and total anesthesia time as predictors of blood loss (21).

Cardiac surgery

In a retrospective study in cardiothoracic surgery on cardiopulmonary bypass (CPB), increased BMI, and preoperative hemoglobin levels were associated with reduced use of PRBC, whereas a higher EuroSCORE (European System for Cardiac Operative Risk Evaluation), longer CPB duration, and a higher fluid balance at 6 hours after surgery were correlated to an increased use of red blood cells (22). Intraoperative body temperature had no impact on red blood cell requirements (22). These findings might be of particular interest for the numerous patients undergoing lung transplantation on CPB.

Predictors of blood loss during lung transplantation

Lung transplantation is a well-established procedure for end stage lung diseases and has been studied thoroughly. However, the predictors of blood loss during the procedure have not been investigated thoroughly so far.

Triulzi *et al.* showed that transplantations on CPB, required more perioperative blood products (23). They found less transfusion requirements in single-lung procedures independent of CPB use. This was attributed to the greater surgical complexity of double compared to single-lung transplantations. In addition, the use of CBP is more frequent during double-lung transplant procedures.

Wang and colleagues confirmed the results of Triulzi (23) and demonstrated less requirement of PRBC, FFP, and platelets during lung transplantation in single-lung transplantation (5). Furthermore, they discovered that the patient's diagnosis had an impact on the amount of blood products required. Eisenmenger's syndrome, a severe form of pulmonary hypertension, and CF patients more frequently needed perioperative blood products, partly because these patients require a double lung transplant. Moreover, many Eisenmenger's syndrome and CF patients have previously undergone cardiac or thoracic surgery, thus these two subgroups often underwent re-sternotomy, which is associated with increased blood loss (24). In the same study, adhesions have been referred to contribute to increased blood loss. Vascularized adhesions are common in CF patients. They are a result of long lasting inflammatory processes and contribute to a higher blood loss complicating surgery (6,25).

Many lung-transplant candidates present with low cardiac output, refractory hypoxemia, and other cardiopulmonary instabilities. Thus, extracorporeal circulation support may be quite commonly required in the form of CPB or extracorporeal membrane oxygenation (ECMO). CPB during pulmonary transplantation increases the risks of early graft dysfunction and bleeding (26-28). The impact of ECMO on blood loss needs to be established. There are studies that suggest ECMO might provide a better view in the operation field for the surgeon, and therefore contribute to less transfusions (29,30), however, there are also contradictory studies that held ECMO to be responsible for blood loss and blood transfusion requirements (31), while other studies do not show any difference between CPB and ECMO (32). Hence, the role of extracorporeal circulation

support in blood loss in lung transplantations is not yet completely understood.

Discussion

Preventing and reducing blood loss decreases morbidity and mortality in surgery and leads to shorter hospitalization (33). The resulting economic impact cannot be neglected.

Although survival rates, surgical techniques and management of bleeding in lung transplantation have improved over the years and although awareness of severe adverse effects of allogeneic blood product transfusion has grown, significant predictors of blood loss have been sparsely identified.

Double-lung transplant is associated with an extended use of blood products when compared to single-lung procedures. This may be a result of longer duration and augmented complexity of surgery. The underlying disease, Eisenmenger's syndrome and CF have also impact on blood loss, due to the reasons discussed previously. The impact of extracorporeal circulation support on blood loss remains contradictory.

Other potential predictors, for instance BMI, preoperative hemoglobin, hematocrit, INR, total surgical and anesthesia time, or risk scores such as the Charlson Comorbidity Index and other important variables of hematology have been investigated in other settings and should be evaluated for lung transplant surgery (34).

Once the risk factors are identified, strategies can be developed, that either target the risk factors or specific steps of the lung transplant procedure in order to minimize blood loss and finally improve patient outcome.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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